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25 February 2020

The Manager Companies  
ASX Limited  
20 Bridge Street  
Sydney NSW 2000

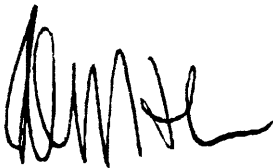
(3 pages by email)

Dear Madam

**SHAREHOLDER UPDATE**

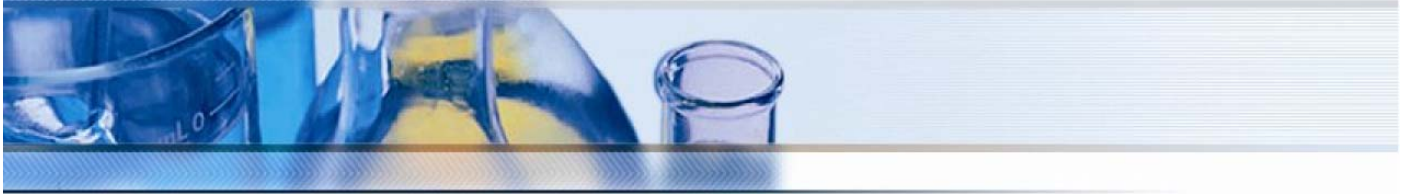
In accordance with Listing Rule 3.17, I attach a copy of a document as sent to the Company's shareholders.

Yours sincerely



Peter J. Nightingale  
Company Secretary

pjn10269



February 2020

Dear Shareholders,

The first weeks of 2020 have certainly been eventful from the perspective of global infectious diseases.

As a developer of drugs targeting significant viral diseases, it was perhaps inevitable that Biotron found itself caught up, in January, in speculation surrounding the outbreak in China of a mysterious coronavirus. As reported in the mass media, this new coronavirus, recently named Covid-19, has caused an international outbreak of respiratory illness.

### **Biotron and Coronavirus**

Biotron develops anti-viral drugs. The Company has had a long interest in coronaviruses. Biotron scientists were the first to identify and characterise a protein found in all coronaviruses and have shown that, by targeting this protein, the virus could be inactivated.

Biotron has compounds that have shown very good activity against several different coronaviruses. These include common human coronaviruses that are one of the major causes of what people classify as 'colds.' Mild respiratory infections can cause serious problems in people with underlying health conditions. Biotron owns a family of compounds that certainly have future potential to be a 'pan-respiratory' treatment for that kind of infection.

As scientists in Australia and internationally have isolated the Covid-19 virus and grown it in cell culture, Biotron can now progress to testing its compounds to see if they can inhibit growth of this new coronavirus. This work will be undertaken in specialist laboratories that have access to Covid-19.

Of course, we hope that this outbreak will be short lived and that the containment processes put in place by governments and other agencies will prevent development of a pandemic. An analogy is the 2002–2004 outbreak of severe acute respiratory syndrome (SARS), which also appeared in China. As it happens, SARS was also a coronavirus – and the current Covid-19 coronavirus belongs to the same family. Some of Biotron's compounds showed activity against SARS. But SARS disappeared relatively quickly and was not, in the end, a commercial target for therapeutics – so we did not pursue that work.

However, given Biotron's expertise in antiviral drug development, including coronaviruses, and uncertainty regarding the likely extent of the outbreak, an assessment of activity of the Company's compounds against Covid-19 is progressing as quickly as possible. We caution that this is not a fast process and it is important that the work is done carefully.

### **HIV-1 Program Update**

As shareholders will know, in September 2018 Biotron announced a successful outcome to the Phase 2 human trial of its lead antiviral drug BIT225 in HIV-1-infected people in combination with current antiretroviral drugs. The results showed that there were significant immunological benefits in patients receiving antiretroviral drugs with 200 mg BIT225, compared to antiretroviral drugs plus placebo.

While current antiretroviral drugs are extremely efficient at clearing the HIV-1 virus, they do not clear cellular reservoirs: because of this, HIV-infected people have to take drugs for their lifetime to keep virus under control.

The trial results Biotron announced in September 2018 showed for the first time that there may be a way to clear cellular reservoirs, which could represent a major step to the ultimate goal of curing HIV-1 infection.

Since completing the Phase 2 HIV-1 clinical trial, Biotron has continued to characterise the unique mechanism of action of BIT225. This has involved detailed post-trial analyses of trial samples. These analyses now provide key information on how BIT225 induces the significant beneficial immunological changes observed in the completed Phase 2 clinical trial.

This work forms the basis of the latest data that the Company will present at the Conference on Retroviral and Opportunistic Infections (CROI), to be held in Boston, USA, in March 2020 (as announced on 3 December 2019). CROI is the pre-eminent international HIV-1 conference and brings together top basic, translational and clinical researchers from around the world to share the latest studies and developments in the ongoing battle against HIV/AIDS and related infectious diseases.

#### **Hepatitis B Virus Program Update**

In addition to its HIV-1 clinical program, Biotron continues to progress its Hepatitis B virus (HBV) program. In pre-clinical studies in cell culture models, Biotron's compounds have demonstrated significant anti-viral activity against HBV, reducing levels of cccDNA (covalently closed circular DNA), as well as other key viral markers. Biotron's compounds have a unique mechanism of action and are expected to generate significant interest from potential partners in Biotron's family of compounds.

We are currently characterising the mechanism of action of the HBV compounds and moving to select a lead drug candidate to take forward to safety studies as quickly as possible.

#### **New Intellectual Property**

These two programs – BIT225 in HIV-1, and the HBV work – are the Company's priorities.

In both programs and on an ongoing basis, further and deeper analysis of the data yields fresh information that augments Biotron's intellectual property.

New data from the Phase 2 trial has resulted in the filing of two new patent applications, expanding the use of BIT225 and other Biotron anti-HIV-1 compounds.

In addition, Biotron has engaged an international contract research organisation to complete chronic toxicology studies of BIT225, to enable the long-term human dosing required for the next stage of clinical development.

#### **Biotron's Broad Antiviral Platform**

Biotron's flagship programs, HIV-1 and HBV, take priority; but we understand that the present high level of focus on coronaviruses necessarily brings attention to the fact that Biotron has a portfolio of antiviral compounds that are active against a much broader range of viruses, including coronaviruses.

We are constantly working on understanding the possible applications of our antiviral platform and continue to work on designing new drugs that target a class of virus protein known as viroporins, which have a key role in the life cycle of a very broad range of viruses. These could have applications in treating viruses, many of which have caused worldwide health issues such as Dengue, Ebola, Middle East Respiratory virus (MERS-CoV), the Zika virus, as well as influenza.

The current interest in the new Covid-19 coronavirus does highlight that Biotron's biotechnology platform represents a way to target a broad range of viruses – including the coronaviruses – and makes our technology and our library of compounds more valuable than is generally understood.

Regards,



**Michelle Miller**  
**CEO & Managing Director**

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